

**1. AMENDMENTS IN THE SPECIFICATION:**

Please replace paragraph 6, at page 5, line 17 with the following amended paragraph:

Even more preferably the compound has a receptor affinity  $IC_{50} < 25 \mu M$ , and an antagonist potency  ~~$IC_{50} < 25 \mu M$~~   $IC_{50} < 1 \mu M$ .

Please replace paragraph 4, at page 8, line 28 with the following amended paragraph:

An "uncommon" amino acid includes, but is not restricted to, D-amino acids, homo-amino acids, N-alkyl amino acids, dehydroamino acids, aromatic amino acids other than phenylalanine, tyrosine and tryptophan, ortho-, meta- or para-aminobenzoic acid, ornithine, citrulline, canavanine, norleucine,  ~~$\beta$ -glutamic~~  $\beta$ -glutamic acid, aminobutyric acid, L-fluorenylalanine, L-3-benzothierylalanine, and  $\alpha, \alpha$ -disubstituted amino acids.

Please replace paragraph 4, at page 12, lines 22 and 25 with the following amended paragraph:

In assays performed at  ~~$4 \pm 4^{\circ}C$~~   $4^{\circ}C$ , buffer, unlabelled human recombinant C5a (Sigma) or peptide, Hunter/Bolton labelled  $^{125}I$ -C5a ( $\sim 20$  pM) (New England Nuclear, MA) and PMNs ( $0.2 \times 10^6$ ) are added sequentially to a Millipore Multiscreen assay plate (HV 0.45) having a final volume of 200  $\mu L$ /well. After incubation for 60 min at  ~~$4 \pm 4^{\circ}C$~~   $4^{\circ}C$ , the samples are filtered and the plate washed once with buffer.

Please replace paragraph 6, at pages 12-13, line 34 and line 2 with the following amended paragraph:

Cells are isolated as previously described (Sanderson *et al*, 1995) and incubated with cytochalasin B (5µg/mL, 15 min, 37°C). Hank's Balanced Salt solution containing 0.15% gelatin and peptide is added on to a 96 well plate (total volume 100 µL/well), followed by 25 µL cells (4x10<sup>6</sup>/mL). To assess the capacity of each peptide to antagonise C5a, cells are incubated for 5 min at 37°C with each peptide, followed by addition of C5a (100 nM) and further incubation for 5 min. Then 50 µL of sodium phosphate (0.1M, pH 6.8) is added to each well, the plate was cooled to room temperature, and 25 µL of a fresh mixture of equal volumes of dimethoxybenzidine (5.7 mg/mL) and H<sub>2</sub>O<sub>2</sub> (0.51%) is added to each well. The reaction is stopped at 10 min by addition of 2% sodium azide. Absorbances are measured at 450 nm in a Bioscan 450 plate reader, corrected for control values (no peptide), and analysed by non-linear regression.

Please replace paragraph 2, at page 21, line 11 with the following amended paragraph:

#### Example 7

#### Postoperative anti-inflammatory treatment

In the experiments involving the surgical severing of the cruciate ligament in dogs, ~~described~~described in Example 3, it was noted that dogs treated with PMX53 recovered from surgery more rapidly than placebo-treated dogs. Dogs undergoing routine orthopaedic surgery, for example for repair of ruptured cruciate ligaments, repair of luxated patella and removal of damaged menisci, are frequently given NSAIDs postoperatively to reduce inflammation and reduce pain. A blinded study with PMX53 and a NSAID such as meloxicam

is performed to test whether PMX53 is effective in managing postoperative pain and in improving outcomes after surgery. This trial is performed in a specialist orthopaedic veterinary practice in order to have access to suitable dogs which are undergoing routine surgery.

Please replace paragraph 3, at page 21, line 24 with the following amended paragraph:

The cyclic compounds described in this specification are stable to proteolytic degradation for at least several hours at ~~37~~37°C in human blood or plasma, in human or rat gastric juices, or in the presence of digestive enzymes such as pepsin, trypsin and chymotrypsin.